

# Respiratory Effects of Environmental Tobacco Smoke in a Panel Study of Asthmatic and Symptomatic Children

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The effect of environmental tobacco smoke (ETS) on respiratory health was investigated among 7- to 12-yr-old children with asthmatic ( $n = 74$ ) or cough ( $n = 95$ ) symptoms. For 3 mo the children measured their peak expiratory flow rate (PEFR) every morning and evening, and kept a daily diary of respiratory symptoms. They also noted daily whether they had used respiratory medication and whether someone had smoked inside their home. Eleven percent of the asthmatic children and 14% of the children with cough had exposure to ETS at home during the study. In multiple regression and analyses controlling for potential confounders, any exposure to ETS during the study was associated with a reduction of 42 L/min (95% confidence interval [CI]: 10 to 74 L/min) in morning and 41 L/min (95% CI: 8 to 74 L/min) in evening PEFR among asthmatic children. Among these children, a dose-dependent increase in the effect of ETS was also seen. Daily variation in ETS exposure was only weakly ( $-9.2$  L/min; 95% CI: 2.9 to 21.2 L/min) associated with PEFR, but the previous day's ETS exposure was a risk factor for bronchodilator use (relative risk [RR]: 10.3; 95% CI: 1.3 to 83.7), as well as for cough (RR: 12.4; 95% CI: 2.4 to 63.3) and phlegm production (RR: 7.8; 95% CI: 1.4 to 41.7), on any given day. Among children with cough only, there was only a weak suggestion of any possible ETS effect. In conclusion, we found that exposure to ETS was associated with a decline in peak flow and increases in respiratory symptoms and use of bronchodilator drugs among asthmatic children. Schwartz J, Timonen KL, Pekkanen J. Respiratory effects of environmental tobacco smoke in a panel study of asthmatic and symptomatic children.

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Exposure to environmental tobacco smoke (ETS), especially from maternal smoking, has been shown to be a risk factor for asthma and wheezing in children (1, 2). It has been estimated that in the population of the United States, maternal smoking is responsible for approximately 7.5% of the total number of cases of childhood asthma or lower respiratory illness marked by wheezing (3).

Children exposed to passive smoking have been reported

to have reduced lung function and to be more often bronchially hyperresponsive (4-8). It has also been suggested that passive smoking is a contributing factor to the development and persistence of airflow limitation in wheezing children (9). On the other hand, 1-h exposure to passive smoking was not associated with consistent changes in lung function or bronchial responsiveness in children with mild bronchial asthma (10, 11).

In an Italian study, passive smoking by children increased the amplitude of the normal circadian rhythm of airway caliber measured with a spirometer (12). Moreover, in a German study, exposure to maternal smoking increased the variability of peak expiratory flow rate (PEFR) among nonasthmatic and asthmatic nonatopic children (13). Few studies have investigated the relationship between ETS and bronchodilator use. Many studies have been cross-sectional rather than longitudinal in design. These two study designs have different potentials for confounding, but they also address different questions about the effects of ETS exposure. Effects found in cross-sectional studies are predominantly effects of chronic exposure. Longitudinal studies provide the opportunity to also address acute responses to ETS exposure.

We studied the association of ETS exposure with PEFR, bronchodilator use, and respiratory symptoms in a panel study of school children in Kuopio, Finland during the winter and spring of 1994. We also compared the estimated acute and chronic effects of ETS on PEFR in these subjects.

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## METHODS

The study was a diary study that examined the correlation of day-to-day changes in PEFr, bronchodilator use, and respiratory symptoms with ETS exposure in school children. The details of the study design are described subsequently.

### Study Population

The study was conducted in Kuopio, a town of 80,000 inhabitants in eastern Finland. In September 1993, a screening questionnaire on respiratory symptoms was distributed through their schools to 2,995 primary-school children in five schools in the center of Kuopio and in three schools in two suburbs of Kuopio (14). The questionnaire was completed and returned by parents of 2,564 children (86%). The 229 children with chronic respiratory symptoms identified by the screening questionnaire, from four schools in the center of Kuopio and from two schools in the suburb of Petonen, were asked to participate in the study. One hundred and ninety-seven of these children agreed to participate.

Chronic respiratory symptoms included wheezing in the preceding 12 mo, attacks of shortness of breath with wheezing in the preceding 12 mo, dry cough during the night and apart from colds in the previous 12 mo, and ever doctor-diagnosed asthma (15). Children who had suffered from wheezing or attacks of shortness of breath with wheezing, or who had doctor-diagnosed asthma, are referred as asthmatic children. Children who had a dry cough as their only respiratory symptom are referred to as children with cough only. At the beginning of the study there were 45 children with asthma and 55 children with cough only in the urban panel, and 41 children with asthma and 57 children with cough only in the suburban panel. Because only children who had valid diary data on more than 60% of the possible days were included in the study analyses, the final sample size was 74 children with asthma and 95 children with cough only.

All children were characterized with skin prick tests and spirometry (15). Skin prick tests were done with the ALK skin prick test allergen panel (ALK Laboratories, Denmark). The allergens tested were birch, common alder, timothy grass and mugwort pollens, cat and dog epithelial danders, and house dust mite (*Dermatophagoides pteronyssinus*). A mean wheal diameter of 2 mm or more was regarded as a positive result if there was no wheal reaction exceeding 1 mm in the negative control (15). A child was defined as atopic if any of the skin prick tests were positive. Before the diary study, parents also filled in a questionnaire, on home characteristics and other factors, including years of full-time education of the father of the child.

### Diary Study

In the winter of 1994, the study subjects were followed for 3 mo. Every morning and every evening they measured their peak expiratory flow rate PEFr three times while in the standing position, using a mini-Wright Peak Flow meter (Airmed; Clement Clarke International Ltd., Essex, UK), before taking any respiratory medication. All three PEFr readings were noted in a diary, and the largest of these three readings was used for data analyses. Respiratory symptoms and amount and type of daily medication for respiratory symptoms, as well as daily

exposure to passive smoking, were also noted in the diary. The latter was investigated with the question "Did anyone smoke inside the home (yes or no)?" (15).

Before the follow-up, four evening meetings (January 31 to February 3, 1994) were arranged at schools to instruct the children and their parents on how to use the mini-Wright Peak Flow meter and on how to fill in the diary. The children and parents who could not attend any of these meetings were instructed personally at a later date. To accommodate learning effects on PEFr measurements, the study period for analyses started on February 8. At least the first 2 d of the diary of each child were excluded for children starting the study later than February 6. The follow-up continued until April 30, 1995.

During the first week of the follow-up period, field workers visited the children at the schools to ensure that the breathing technique used in PEFr measurements was proper and that the children understood how to fill in the diaries. After that, the field workers visited the children at the schools every 2 wk. During these visits, the completed diaries were collected from the children, new diaries were given for the next 2-wk period, and the functioning of the peak flow meters was checked.

Daily temperature and humidity data were obtained from the weather station network of the City of Kuopio.

### Analytical Methods

**Peak expiratory flow.** Two types of analyses were performed. In the first analysis we focused on the effects of chronic exposure to ETS. Subjects were classified as either ever exposed or never exposed on the basis of their responses in the daily diaries, and we examined whether children who had ETS exposure had lower than expected PEFrs. The association between ETS exposure and peak flow levels was investigated through multiple regression analysis (16), with two types of control variables. Time-independent cofactors included age, height, gender, atopic status, weight, father's years of education, and use of maintenance drugs (inhaled corticosteroids, sodium cromoglycate, or nedocromil sodium). Time-dependent covariates included day of study (to account for increase in the children's peak flow over time), previous day's temperature and humidity, bronchodilator use, and whether or not the measurement was taken on a weekend. A completely cross-sectional analysis computed a mean value for morning and evening PEFr for each child, and regressed this against the time-invariant covariates and ETS exposure, weighting by the inverse of the variance of the mean PEFr. This analysis ignored the contributions of the time-dependent covariates in explaining some of the variation about children's mean PEFrs.

To make better use of our data, we also performed analyses of the chronic effects of ETS exposure, which used child-day as the unit of observation, and included all the time-dependent covariates. However, each observation is not independent in such an analysis. A child whose PEFr is higher than expected for the child's height and age in one observation is likely to be higher than average in most of the child's other PEFr measurements. To deal with this correlation, we used a random subject effect in the Proc Mixed protocol of the SAS software system (SAS Institute, Cary, NC). The analyses were performed separately for the asthmatic cohort and the cough-only cohort.

TABLE 1

PERCENTILES OF DISTRIBUTION OF CONTINUOUS  
VARIABLES IN 74 ASTHMATIC CHILDREN

Variable	10%	25%	50%	75%	90%	Mean	Child-Days
Morning PEF, L/min	245	300	340	390	425	338	5,073
Evening PEF, L/min	250	300	340	395	430	342	5,153
Height, cm	126	130	138	145	153	138	5,978
Weight, kg	25	29	35	42	50	36	5,978
Age, yr	7	8	9	11	12	9.55	6,060
Relative humidity, %	58	67	76	82	87	74	5,986
Minimum temperature, °C	-17	-12	-3	0	2	-5.5	5,986
DiffPEF, L/min	-20	-10	0	10	30	3.4	4,932

Definition of abbreviations: DiffPEF = difference between morning and evening PEF; PEF = peak expiratory flow.

TABLE 2

PERCENTILES OF DISTRIBUTION OF CONTINUOUS  
VARIABLES IN 95 CHILDREN WITH COUGH ONLY

Variable	10%	25%	50%	75%	90%	Mean	Child-Days
Morning PEF, L/min	260	330	340	380	425	343	5,877
Evening PEF, L/min	270	305	350	385	430	347	6,030
DiffPEF*, L/min	-20	-10	0	10	25	3.4	5,651
Height, cm	123	130	139	145	154	138	7,297
Weight, kg	25	27	32	40	47	34.3	7,856
Age, yr	7	8	9	11	12	9.5	7,143
Relative humidity, %	58	67	77	82	88	75	7,297
Minimum temperature, °C	-18	-12	-4	0	2	-6.2	7,297

Definition of abbreviations: DiffPEF = difference between morning and evening PEF; PEF = peak expiratory flow.

TABLE 3  
MEAN PERCENT OF CHILDREN (OR CHILD-DAYS) WITH DICHOTOMOUS CHARACTERISTICS

Variable	Asthmatic Children (n = 74)		Children with Cough Only (n = 95)	
	Percent of Children	Percent of Child-Days	Percent of Children	Percent of Child-Days
Female	39.2	39.2	49.5	49.5
ETS exposure	10.8	10.8	15.8	15.8
High ETS	4.1 <sup>†</sup>	4.0	7.4	7.4
Some ETS	6.8	6.7	8.4	8.4
Atopy	75.7	75.6	54.7	54.8
Bronchodilator use	40.5*	18.9	NA	NA
Maintenance drugs	2.0	1.9	NA	NA
Father a high-school graduate	47.3	47.3	48.4	48.4
Cough	90	28.3	88	28.2
Phlegm production	77	18	70	13.9
Wheezing	45	4.4	27	3.2
Breathing difficulty	45	5.6	28	3.9

Definition of abbreviation: ETS = environmental tobacco smoke.

\* Any use during study period.

<sup>†</sup> > 10% of days.

To investigate the shape of the dose-response curve, children with ETS exposure were divided into those exposed for more than 10% of the time and those with exposure on 10% or fewer days. This roughly divided the number of exposure days in half.

The second approach focused on the acute effects of ETS exposure on the previous one or two days on the current day's peak flow. This can only be addressed in a time-series study. We repeated the regression analysis with the previous day's ETS as our exposure measure, and in this case included an indicator variable for each child, rather than a random-child effect. The use of dummy variables for each child prevents any differences among children in overall exposure to ETS from contributing to the regression coefficient. Hence, in these regressions, only day-to-day variation in ETS exposure could correlate with peak flow. Because the use of dummy variables for each child also removed the effect of the time-independent factors (which only vary across a single child), these regressions included all of the time-dependent covariates along with the child-specific dummy variables.

**Respiratory symptoms and bronchodilator use.** There is reason to believe that symptom-reporting rates might vary between homes with and without ETS exposure. To minimize the potential for bias, we restricted our analysis of symptoms and bronchodilator use to acute effects of ETS exposure only. We fit logistic regression models to investigate the association between ETS exposure and daily reports of bronchodilator use or respiratory symptoms. These were longitudinal models, examining the association between the same day's or immediately prior day's exposure to ETS and symptom reporting or bronchodilator use. Once again, dummy variables were included for each child in order to control for unmeasured covariates across child. By controlling for mean differences across subjects, and examining, conditional on the number of events a subject reported, the events were more likely to occur after acute exposure, we focused our analysis only on the acute effects of ETS. These regressions controlled for the same covariates named earlier (except for the regression on bronchodilator use).

## RESULTS

Tables 1 to 3 show the distribution of the data for asthmatic and nonasthmatic children. On average, asthmatic children had morning PEFRs that were slightly lower than those of children with coughing alone in the screening questionnaire. ETS exposure at home was relatively rare in our samples, with only 11% of the asthmatic children and 14% of the children with coughing symptoms alone having any exposure. The asthmatic children were more likely to be male (61%) than were the other children (50%).

## Asthmatic Childrens' PEFR Results

In a cross-sectional model for morning PEFR, any ETS exposure at home was associated with a reduction of 43.9 L/min (95% confidence interval [CI]: 15.3 to 72.5). When we analyzed the data longitudinally, including a random-subject effect, ETS exposure at home was associated with a reduction in PEFR of 41.9 L/min (95% CI: 9.5 to 74.3 L/min) after controlling for age, height, sex, atopic status, father's education, weight, use of maintenance drugs, day of study, previous day's temperature and humidity, bronchodilator use, a random-subject effect, and whether the measurement was taken on a weekend. To assess the potential for confounding by socioeconomic status, atopic status, bronchodilator use, and use of maintenance drugs on the ETS association, we examined the effect of deleting these variables from the model (one at a time). Table 4 shows the ETS effect in these different models. Overall, little evidence for confounding was seen. However, there was some indication of negative confounding with socioeconomic status. That is, failure to control for father's years of education resulted in a lower estimate (26 L/min; 95% CI: -4.7 to 56.6) of the ETS-related decline in PEFR.

Evening PEFR was also lower in the asthmatic children with ETS exposure at home (Table 4). These results were also

TABLE 4  
EFFECTS OF ENVIRONMENTAL TOBACCO SMOKE  
EXPOSURE AT HOME ON PEAK FLOW WITH AND  
WITHOUT CONTROL FOR VARIOUS POTENTIAL  
CONFOUNDERS IN 74 ASTHMATIC CHILDREN

Model	Morning PEFR (Range) (L/min)	Evening PEFR (Range) (L/min)
Cross-sectional	-43.9 (-15.3, -72.5)	-39.4 (-10.0, -68.8)
Longitudinal analysis		
Baseline*	-41.9 (-9.5, -74.3)	-40.7 (-7.6, -73.7)
No maintenance drugs	-42.7 (-9.8, -75.6)	-41.2 (-7.9, -74.6)
No father's educational level	-26.0 (4.7, -56.6)	-23.8 (7.4, -55)
No atopy	-41.1 (-9.0, -73.2)	-40.3 (-7.6, -72.9)
No bronchodilator use	-43.5 (-11, -76)	-42 (-8.8, -75.1)

Definition of abbreviations: PEFR = peak expiratory flow.

\* Adjusting for age, height, gender, atopic status, father's educational level, weight, use of maintenance drugs, day of study, bronchodilator use, previous day's temperature and humidity, weekend, and a random-subject effect.

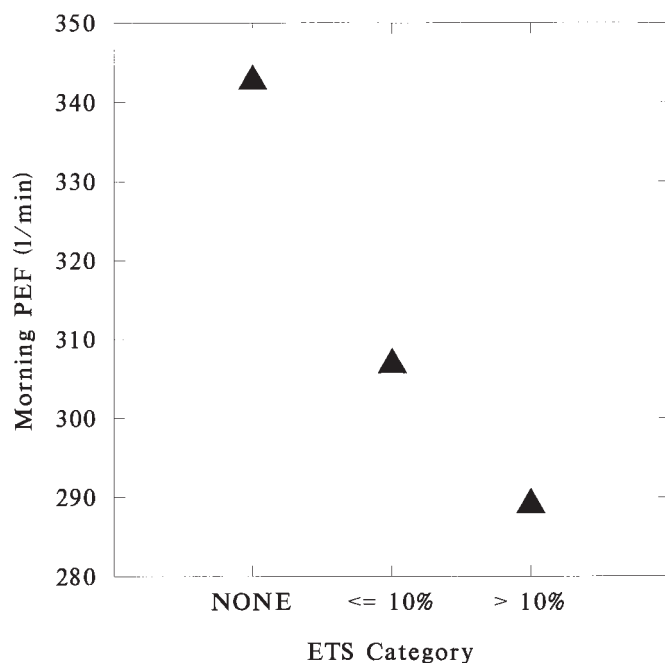


Figure 1. Covariate adjusted morning PEFR versus percent of days with ETS exposure in asthmatic children. The covariates for which adjustments were made were age, height, gender, atopic status, father's educational level, weight, and use of maintenance drugs.

insensitive to control for atopic status or drug use, but failure to control for socioeconomic status masked some of the effect.

Evidence was also seen for a dose-dependent increase in the effect of ETS as the amount of ETS exposure increased. Figure 1 shows the decrease in morning PEFR in children with some ETS exposure and with high ETS exposure versus children with no ETS exposure, after control for covariates. Here, high ETS exposure refers to our high category, and is not meant as a normative statement. A test for trend was significant ( $p = 0.01$ ). Similar results were seen for evening PEFR (results not shown).

In time-series regressions with dummy variables for each child, the previous day's ETS exposure tended to be associated with morning PEFR (9.2 L/min decline; 95% CI:  $-2.9$  to  $21.2$  L/min;  $p = 0.14$ ), but the association was not significant.

#### Bronchodilator Use and Respiratory Symptoms

Symptoms of cough and phlegm production were much more common in the asthmatic children than were wheezing or breathing difficulties as recorded in the childrens' diaries (Table 3). Given those small numbers, it was not possible to analyze the association of wheezing or breathing difficulties with ETS exposure. Bronchodilator use was moderate, at about 20% of child days.

The previous day's ETS exposure was a significant risk factor for need for bronchodilator use on any given day (Table 5). Coughing and phlegm production were also associated with ETS exposure. For these symptoms, the mean ETS exposure over the previous 2 d was a stronger predictor than was the previous day's exposure.

#### Results for Children with Cough Alone

ETS-exposed children in the subgroup with cough alone also had lower PEFR values in both the morning (11.3 L/min lower; 95% CI:  $-12.6$  to  $35.2$ ) and evening (13.6 L/min lower; 95% CI:  $-10.7$  to  $37.9$ ), but the association was far from sig-

TABLE 5

ODDS RATIOS FOR BRONCHODILATOR USE AND RESPIRATORY SYMPTOM REPORTING IN ASTHMATIC CHILDREN ASSOCIATED WITH ENVIRONMENTAL TOBACCO SMOKE EXPOSURE ON THE PREVIOUS DAY (BRONCHODILATOR USE), OR WITH MEAN EXPOSURE ON THE PREVIOUS 2 d (SYMPTOMS)

Event	OR	95% CI
Bronchodilator use	10.3	1.3–83.7
Cough	12.4	2.4–63.3
Phlegm production	7.8	1.4–41.7

Definition of abbreviations: CI = confidence interval; OR = odds ratio.

nificant, and the magnitude of the effect was about a quarter of that seen in the asthmatic children. Bronchodilators were not used by this cohort, and symptoms were more rare, and no analyses of these outcomes were therefore done.

#### DISCUSSION

Asthmatic children with *chronic* ETS exposure had lower peak flows in this study. These changes showed evidence of a dose-dependent effect, with children who were exposed for a greater proportion of time having greater reductions in PEFR. Bronchodilator use was also greater among asthmatic children with ETS exposure. Social class, atopic status, and use of regular medication did not confound these associations. However, the evidence that the effects of ETS on PEFR manifested themselves immediately was weak. There was a suggestion of a decrease in morning PEFR following the day of ETS exposure, but not a very strong one. Leaving aside the significance of the observed effect, which may reflect low power due to the small number of person-days of ETS exposure, the magnitude of the *acute* change in PEFR following ETS exposure was considerably smaller than the observed association with chronic exposure. We should note that this regression controlled for each individual child, and therefore reflects the *average chronic effect* of ETS exposure. This suggests that any additional effect of *acute* exposure is likely to have been small.

The association between bronchodilator use and ETS exposure on the previous day is quite suggestive. If children increased their use of bronchodilator medication following *acute* ETS exposure, one would expect this to mute the association between *acute* ETS exposure and PEFR. A similar effect was noted by Pope and colleagues (17) in a diary study in a Utah valley. They reported an association between particulate air pollution and use of bronchodilator medication in a panel of asthmatic subjects, but no association between particulate air pollution and peak flow changes in that panel. They interpreted this as suggesting that medication use removed the potential link between exposure and PEFR.

The association between ETS exposure on the previous 2 d and reports of cough and phlegm production is also indicative of an *acute* response to ETS. Again the analogy with air pollution is interesting. Coughing symptoms have been more frequently reported to be associated with air pollution than have any other symptoms.

Overall, we believe our findings are supportive of an *acute* effect of ETS exposure on asthmatic children, in addition to a more *chronic* effect. The weaker and insignificant association in the nonasthmatic cohort suggests that healthier children are less affected by ETS exposure. This same difference between the response of asthmatic and nonasthmatic children has also been observed for air pollution in this cohort (18).

A number of limitations must be pointed out in this study. First, the number of children with ETS exposure was not large,

nor was the number of child days of exposure. The primary effect of this limitation is to reduce the power to find an association, and this may have influenced our regressions of day-to-day effects of ETS exposure. On the other hand, the small number of children in our study cohort increases the risk of accidental confounding with omitted covariates in the cross-sectional models. This does not apply to the regressions that had dummy variables for each child.

A number of potential confounders have been suggested by several authors (19). Prominent among them is socioeconomic status. Our panel of asthmatic children was relatively high in social status, with about half of the fathers having more than a high-school education. Control for father's years of education actually increased the estimated effect of ETS exposure, rather than decreasing it. This suggests that the fears that reported associations reflect such confounding are unrealized. The effects of ETS were not confounded by atopy, nor by differences in the use of maintenance medication between children with and without exposure. This does not mean that there may not be other uncontrolled confounders, however.

Another major issue is the possibility that current ETS exposure is correlated with ETS exposure during pregnancy. A number of cross-sectional studies have reported associations between ETS exposure during pregnancy and either the development of asthma (20) or lower FEF<sub>25-75</sub> later in life (21). Some studies have indicated that the effects of current ETS exposure at home disappear after control for this risk factor (21). Unfortunately, these data were not available in our analysis. Several pieces of evidence suggest that ETS exposure during pregnancy probably does not explain all of our findings. First, we found a dose-response relationship with the number of days of ETS exposure recorded in our subjects' diaries. It would be remarkable if the amount of ETS exposure during pregnancy was so highly correlated with the amount of ETS exposure almost 10 yr later as to account for this finding. In addition, in regressions that controlled for each child's individual risk, a significant association was found between the prior day's ETS exposure and bronchodilator use, coughing, and phlegm production, and a trend toward an association was found between the prior day's ETS exposure and morning PEFR. These associations cannot possibly have been confounded by ETS exposure during pregnancy, since differences in such a past history between children will be controlled by the individual child dummy variables.

Although this study reports effects of ETS exposure on peak flow, medication use, and respiratory symptoms, the crudeness of our exposure measure limits the ability to generalize the specific effect-size estimates. Specifically, we did not have any data on the number of cigarettes smoked in the home on days with exposure, and this could differ in other populations. Hence, the expected effect on peak flow may also differ in those populations.

In conclusion, exposure to ETS was associated with a decline in peak flow and increase in symptom reporting and use of bronchodilator drugs by asthmatic children. The effect of ETS on PEFR in this study was largely chronic, but evidence for an effect of daily variations in ETS was seen for bronchodilator use and respiratory symptoms, and there was a suggestion of an acute effect on PEFR. Ten percent of the children with asthmatic symptoms were exposed to ETS. This proportion may well increase in the future with the increasing prevalence of smoking among women (22). Among unselected children and in other countries, over half of children may be exposed to ETS (20). Therefore, prevention of ETS exposure is still a major factor, in promoting respiratory health, and also among children with asthma.

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